REMARKS

Status of the Claims

Pending claims

Claims 3 to 27 are pending (claims 1 and 2 were canceled in a previous response).

Claims amended and canceled in the instant amendment

Claims 4, 10, 12 to 16 and 20 to 24 are amended, claims 9 and 19 are canceled, without prejudice. Thus, after entry of the instant amendment, claims 3 to 8, 10 to 18, and 20 to 27 will be pending.

The specification

The specification has been amended to indicate that related patent applications USSN 09/443,497, issued as U.S. Patent No. 6,466,874, on October 15, 2002, and USSN 09/493,498, issued U.S. Patent No. 6,564,151, on May 13, 2003.

Claim objections

The Patent Office alleges that claims 9 and 19 are essentially duplicates of claim 3. The instant amendment addresses this issue. Claims 9 and 19 are canceled, without prejudice.

Issues under 35 U.S.C. §112, first paragraph

Enablement

Claims 3 to 27 are rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not reasonably provide enablement for the claimed invention.

The Patent Office notes that the specification is enabling for reasonably determining functional links between certain proteins from a genome by establishing their phylogenetic profiles through finding homologues in additional genomes.

However, it is alleged that the specification does not reasonably provide enablement for determining functional links between a great number other proteins from a genome by establishing their phylogenetic profiles through finding homologues in additional genomes. In particular, it is alleged that because the claims read on significant numbers of inoperative embodiments, including known house-keeping proteins (as discussed in the office action), it would take undue experimentation to identify operative embodiments.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to practice the claimed invention without undue experimentation. The specification enabled the skilled artisan at the time of the invention to identify operative, versus non-operative, embodiments without undue experimentation. The state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., identifying operative embodiments of the invention (i.e., identifying non-homologous proteins as being functionally linked by a "Rosetta Stone" method and identifying pairs of proteins in a genome as being functionally linked by a "phylogenetic profile" method) was very high.

Whether large numbers of non-operative embodiments must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of non-operative embodiments, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also would have recognized the need to screen numbers of negatives to find an operative embodiment of the claimed methods, e.g., identifying functionally-linked proteins. Screening procedures used to identify functionally-linked proteins within the scope of the instant invention were well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could practice the claimed methods without undue experimentation.

Accordingly, Applicants respectfully submit that the pending claims meet the enablement requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §112, second paragraph

Claims 3 to 27 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The term "non-homologous proteins"

The Patent Office alleges that the term "non-homologous proteins" in independent claims 3, 9 and 19 is vague and indefinite because, inter alia, it is unclear how to determine the extent of homology needed to be "non-homologous" verus "homologous."

The legal standard for definiteness under section 112, second paragraph, is whether a claim reasonably apprises those of skill in the art of its scope. See, e.g., In re Warmerdam, 33 F.3d 1354,31 USPQ2d 1754, 1759 (citing Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d at 1217, 18 USPQ2d at 1030). Applicants respectfully note that when claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, they satisfy the requirement of section 112, second paragraph. See, e.g., North American Vaccine Inc. v. American Cyanamid Co., 7 F.3d 1571, 28 USPQ 1333, 1339 (Fed. Cir. 1993). The amount of detail required to be included in claims depends on the particular invention and the prior art, and is not to be viewed in the abstract but in conjunction with

whether the specification is in compliance with the first paragraph of section 112.

The specification clearly provides guidance on the limitations and scope of the term "non-homologous," and expressly defines the term "substantially homologous."

For example, on page 3, lines 4 to 7, the specification notes

> Throughout evolution, the protein sequences in different organisms have been conserved to varying degrees. As a result, any given organism contains many proteins that are recognizably similar to proteins in other organisms. Such similar proteins, having arisen from the same ancestral protein, are called homologs. [emphasis added]

On page 4, lines 12 to 17, the specification notes

> Functionally-linked proteins evolve in a correlated fashion, and therefore they have homologs in the same subset of organisms. For instance, it is expected that flagellar proteins will be found in bacteria that possess flagella but not in other organisms. Simply put, if two proteins have homologs in the same subset of fully (or nearly fully) sequenced organisms but are absent in other organisms they are likely to be functionally-linked. [emphasis added]

On page 15, lines 24 to 28, the specification notes

> "Substantially homologous" means that the p value of the alignment score is statistically significant. A number of publicly available alignment programs can be used to determine the homology including, for example, BLAST and FASTA. A comparison of the polypeptide sequences can be performed to insure that the polypeptides are non-homologous. As a result only proteins having distinct non-homologous polypeptide domains will be used for further analysis. [emphasis added]

Thus, from the teachings and definitions provided in the specification it would have been clear to the skilled artisan the limitations and scope of the term "non-homologous" as used in the claimed methods. The claims, read in light of the specification, reasonably apprised those skilled in the art both of the utilization and scope of the invention.

Accordingly, Applicants respectfully aver that in the context of the invention as a whole the specification reasonably apprised those skilled in the art both of the utilization and scope of the invention with respect to the term "non-homologous."

The term "high confidence"

The Patent Office alleges that the term "high confidence" in independent claims 3, 9 and 19 is vague and indefinite because, inter alia, it is unclear how high a confidence is

needed, and in what measure is considered "high confidence", to identify a functional link between two proteins.

The specification clearly provides guidance on the limitations and scope of the term "high confidence." For example, Figure 10 shows the high confidence functional links found by phylogenetic profiles for the yeast protein YGR021W (see, e.g., page 9, lines 6 to 8, of the specification). Figure 11A shows high and highest confidence functional links established for the yeast prion Sup35 (see, e.g., page 9, lines 9 to 12). Figure 12 shows high and highest confidence functional links found for the yeast DNA repair protein MSH6 (see, e.g., page 9, lines 13 to 14). See also Table III, page 40, describing the prediction of function of yeast proteins, including data coverage and reliability of predictions, including "High Confidence Links," and "Highest Confidence Links," in # of proteins, # of Functional Links, Ability to Predict Known Function, Ability in RandomTrials, and, Signal to Noise.

The specification further notes (after Table III), on page 40, line 23, to page 41, line 2:

> These links provide a means to characterize proteins of unknown function. There are 2,557 uncharacterized proteins in yeast (Mewes et al. Nucleic Acids Res. 26:33-37 (1998)), proteins not studied experimentally and with no strong homologs of known function. Of these, 374, or 15%, can be assigned a general function from the high and highest confidence functional links and 1,524, or 60%, can be assigned a general function using all links. [emphasis added]

Thus, from the teachings and definitions provided in the specification it would have been clear to the skilled artisan the limitations and scope of the term "high confidence" as used in the claimed methods. The claims, read in light of the specification, reasonably apprised those skilled in the art both of the utilization and scope of the invention.

Accordingly, Applicants respectfully aver that in the context of the invention as a whole the specification reasonably apprised those skilled in the art both of the utilization and scope of the invention with respect to the term "high confidence."

The phrase "substantially all protein sequences"

The Patent Office alleges that the phrase "substantially all protein sequences" in independent claims 3, 9 and 19 is vague and indefinite because, inter alia, it is unclear how many

protein sequences encoded by a genome are considered as "substantially all" protein sequences.

The fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. See, e.g., Seattle Box Co., v. Industrial Crating & Packing, Inc., 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. MPEP §2173.05(b), page 2100-202, Rev. 1, Feb. 2003.

The term "substantially" is often used in conjunction with another term to describe a particular characteristic of the claimed invention. It is a broad term. In In re Nehrenberg, 280 F.2d 161, 126 USPQ 383 (CCPA 1960), the court held that the limitation "to substantially increase the efficiency of the compound as a copper extractant" was definite in view of the general guidelines contained in the specification. In re Mattison, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). The court held that the limitation "which produces substantially equal E and H plane illumination patterns" was definite because one of ordinary skill in the art would know what was meant by "substantially equal." Andrew Corp. v. Gabriel Electronics, 847 F.2d 819, 6 USPQ2d 2010 (Fed. Cir. 1988). MPEP §2173.05(b)(D), page 2100-203, Rev. 1, Feb. 2003.

Analogously, the term "substantially" as used in the instant claimed invention is definite because one of ordinary skill in the art, in the context of the specification, would have known what was meant by "substantially all protein sequences." The claims, read in light of the specification, reasonably apprised those skilled in the art both of the utilization and scope of the invention. Accordingly, Applicants respectfully aver that in the context of the invention as a whole the specification reasonably apprised those skilled in the art both of the utilization and scope of the invention with respect to the phrase "substantially all protein sequences."

The term "the genome"

The Patent Office alleges that the term "the genome" in claim 4 lacks antecedent basis, and, the last two steps of claim 4 lack clear connection with the steps of claim 3. The instant amendment addresses these issues.

Issues regarding Double Patenting

Claims 3 and 7 to 27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1 to 19 of U.S. Patent No. 6,466,874, and claims 2 to 8, 11 to 21, 30 to 32 and 34 to 42, of USSN 09/493,498, issued as U.S. Patent No. 6,564,151, on May 13, 2003. An appropriate Terminal Disclaimer addressing this issue is attached.

Claims 4 to 6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1 to 19 of U.S. Patent No. 6,466,874, and claims 2 to 8, 11 to 21, 30 to 32 and 34 to 42 of USSN 09/493,498, issued as U.S. Patent No. 6,564,151, on May 13, 2003, in view of Eisen, et al. (1998) Proc. Natl. Acad. Sci. USA 95:14863-14868. An appropriate Terminal Disclaimer addressing this issue is attached.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, and under the judicially created doctrine of obviousness-type double patenting. Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050. Please credit any overpayment to this account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date: Sept. 26, 2003

Gregory P. Einhorn
Reg. No. 38,440

Fish & Richardson P.C.
4350 La Jolla Village Drive, Suite 500
San Diego, California 92122
Telephone: (858) 678-5070
Facsimile: (858) 678-5099

10332908.doc